

L3 ANSWER 23 OF 47 MEDLINE
 AN 2001173020 MEDLINE
 DN 21120425 PubMed ID: 11208141
 TI Role of P30 in replication and spread of TMV.
 AU Beachy R N; Heinlein M
 CS Donald Danforth Plant Science Center, 7425 Forsyth Boulevard, Box 1098,
 St. Louis, MO 63105, USA.. rnbeachy@danforthcenter.org
 SO TRAFFIC, (2000 Jul) 1 (7) 540-4. Ref: 32
 Journal code: 100939340. ISSN: 1398-9219.
 CY Denmark
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 200104
 ED Entered STN: 20010502
 Last Updated on STN: 20010502
 Entered Medline: 20010426
 AB The P30 movement protein (MP) of tobacco mosaic virus is
 essential for distribution of sites of replication within infected cells
 and for cell-cell spread of infection. MP is an integral membrane protein
 and in early and mid-stages of infection causes severe disruption of the
 cortical endoplasmic reticulum (ER). MP also associates with microtubules,
 and in late stages is targeted for degradation by the 26S
 proteasome. During these stages, the ER regains its normal
 pre-infection configuration. Viral RNA is associated with ER and
 microtubules in the presence of MP. The MP is phosphorylated and mutation
 of the phosphorylated amino acid reduced association of MP with the ER,
 plasmodesmata, and microtubules, and altered the stability of the MP. The
 nature of the association of MP with vRNA and ER and microtubules, and the
 role of phosphorylation of MP in each of these functions, if any, remains
 to be determined.

L3 ANSWER 24 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 2000:390801 BIOSIS
 DN PREV2000000390801
 TI Nasal immunization with subunit proteasome influenza vaccines
 induce enhanced respiratory IgA and serum hemagglutination inhibition
 activity.
 AU Plante, M. (1); Jones, D. (1); Allard, F. (1); Torrossian, K. (1);
 Gauthier, J. (1); White, G. (1); Lowell, G. (1); Burt, D. (1)
 CS (1) Intellivax International Inc., Ville Saint-Laurent, PQ Canada
 SO Abstracts of the General Meeting of the American Society for Microbiology,
 (2000) Vol. 100, pp. 297. print.
 Meeting Info.: 100th General Meeting of the American Society for
 Microbiology Los Angeles, California, USA May 21-25, 2000 American Society
 for Microbiology
 . ISSN: 1060-2011.
 DT Conference
 LA English
 SL English

L3 ANSWER 25 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 2001:199403 BIOSIS
 DN PREV200100199403
 TI Role of protein tyrosine phosphatases in thyroid carcinogenesis.
 AU Fusco, Alfredo (1); Trapasso, Francesco; Iuliano, Rodolfo; Martelli, Maria
 Luisa; Baldassarre, Gustavo; Bruni, Paola; Chiappetta, Gennaro;
 Chiariotti, Lorenzo; Santoro, Massimo; Viglietto, Giuseppe
 CS (1) Dipartimento di Biologia e Patologia Cellulare e Molecolare, Facolta'
 di Medicina e Chirurgia, Universita' degli Studi di Napoli, Napoli Italy
 SO Endocrine Journal, (August, 2000) Vol. 47, No. Suppl. August, pp. 95.

print.

Meeting Info.: 12th International Thyroid Congress Kyoto,, Japan October
22-27, 2000 British Society of Gastroenterology
. ISSN: 0918-8959.

DT Conference
LA English
SL English

L3 ANSWER 26 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 2001:113523 BIOSIS

DN PREV200100113523

TI HIV protease inhibitors protect apolipoprotein B from degradation by the
proteasome: A potential mechanism for protease inhibitor-induced
hyperlipidemia.

AU Liang, Jun-Shan (1); Distler, Oliver (1); Cooper, David A.; Deckelbaum,
Richard J.; Sturley, Stephen L.; Ginsberg, Henry N.

CS (1) Columbia Univ, New York, NY USA

SO Circulation, (October 31, 2000) Vol. 102, No. 18 Supplement, pp. II.149.
print.

Meeting Info.: Abstracts from Scientific Sessions 2000 New Orleans,
Louisiana, USA November 12-15, 2000
ISSN: 0009-7322.

DT Conference
LA English
SL English

L3 ANSWER 27 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE
6

AN 1999:341262 BIOSIS

DN PREV199900341262

TI The human papillomavirus type 16 E6 oncoprotein can down-regulate p53
activity by targeting the transcriptional coactivator CBP/p300.

AU Zimmermann, Holger; Degenkolbe, Roland; Bernard, Hans-Ulrich; O'Connor,
Mark J. (1)

CS (1) KuDOS Pharmaceuticals Limited, Milton Road, 327 Cambridge Science
Park, Cambridge, CB4 4GW UK

SO Journal of Virology, (Aug., 1999) Vol. 73, No. 8, pp. 6209-6219.
ISSN: 0022-538X.

DT Article
LA English
SL English

AB The transforming proteins of the small DNA tumor **viruses**, simian
virus 40 (SV40), adenovirus, and human papillomavirus (HPV) target
a number of identical cellular regulators whose functional abrogation is
required for transformation. However, while both adenovirus E1A and SV40
large T transforming properties also depend on the targeting of the
transcriptional coactivator CBP/p300, no such interaction has been
described for the HPV oncoprotein E6 or E7. Here, we demonstrate that the
HPV-16 E6 protein, previously shown to facilitate the degradation of p53
in a complex with E6-associated protein (E6AP), also targets CBP/p300 in
an interaction involving the C-terminal zinc finger of E6 and CBP residues
1808 to 1826. Furthermore, this interaction is limited to E6 proteins of
high-risk HPVs associated with cervical cancer that have the capacity to
repress p53-dependent transcription. An HPV-16 E6 mutant (L50G) that binds
CBP/p300, but not E6AP, is still capable of down-regulating p53
transcriptional activity. Thus, HPV E6 proteins possess two distinct
mechanisms by which to abrogate p53 function: the repression of p53
transcriptional activity by targeting the p53 coactivator CBP/p300, and
the removal of cellular p53 protein through the **proteasome**
degradation pathway.

L3 ANSWER 28 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1999:154813 BIOSIS

DN PREV199900154813

TI Possible involvement of proteasomes (prosome) in AUUUA-mediated mRNA decay.

AU Jarrousse, Anne-Sophie; Petit, Franck; Kreutzer-Schmid, Claudia; Gaedigk, Roger; Schmid, Hans-Peter (1)

CS (1) Equipe "Proteasome et Auto-Surveillance Cellulaire" OVGU UA INRA 987, Univ. Blaise Pascal, Clermont-Ferrand II, 24 ave. des Landais, 63177 Aubiere Cedex France

SO Journal of Biological Chemistry, (Feb. 26, 1999) Vol. 274, No. 9, pp. 5925-5930.
ISSN: 0021-9258.

DT Article

LA English

AB We have identified a cellular target for proteasomal endonuclease activity. Thus, 20 S proteasomes interact with the 3'-untranslated region of certain cytoplasmic mRNAs in vivo, and 20 S proteasomes isolated from Friend leukemia virus-infected mouse spleen cells were found to be associated with a mRNA fragment showing great homology to the 3'-untranslated region of tumor necrosis factor-beta mRNA that contains AUUUA sequences. We furthermore demonstrate that 20 S proteasomes destabilize oligoribonucleotides corresponding to the 3'-untranslated region of tumor necrosis factor-alpha, creating a specific cleavage pattern. The cleavage reaction is accelerated with increasing number of AUUUA motifs, and major cleavage sites are localized at the 5' side of the A residues. These results strongly suggest that 20 S proteasomes could be involved in the destabilization of cytokine mRNAs such as tumor necrosis factor mRNAs and other short-lived mRNAs containing AUUUA sequences.

L3 ANSWER 29 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 2000:62511 BIOSIS

DN PREV200000062511

TI A dynamic connection between centromeres and ND10 proteins.

AU Everett, Roger D. (1); Earnshaw, William C.; Pluta, Ann F.; Sternsdorf, Thomas; Ainsztein, Alexandra M.; Carmena, Mar; Ruchaud, Sandrine; Hsu, Wei-Li; Orr, Anne

CS (1) MRC Virology Unit, Church Street, Glasgow, G11 5JR UK

SO Journal of Cell Science, (Oct., 1999) Vol. 112, No. 20, pp. 3443-3454.
ISSN: 0021-9533.

DT Article

LA English

SL English

AB ND10, otherwise known as nuclear dots, PML nuclear bodies or PODs, are punctate foci in interphase nuclei that contain several cellular proteins. The functions of ND10 have not been well defined, but they are sensitive to external stimuli such as stress and virus infection, and they are disrupted in malignant promyelocytic leukaemia cells. Herpes simplex virus type 1 regulatory protein Vmw110 induces the proteasome-dependent degradation of ND10 component proteins PML and Sp100, particularly the species of these proteins which are covalently conjugated to the ubiquitin-like protein SUMO-1. We have recently reported that Vmw110 also induces the degradation of centromere protein CENP-C with consequent disruption of centromere structure. These observations led us to examine whether there were hitherto undetected connections between ND10 and centromeres. In this paper we report that hDaxx and HP1 (which have been shown to interact with CENP-C and Sp100, respectively) are present in a proportion of both ND10 and interphase centromeres. Furthermore, the proteasome inhibitor MG132 induced an association between centromeres and ND10 proteins PML and Sp100 in a significant number of cells in the G2 phase of the cell cycle. These results imply that there is a dynamic, cell cycle regulated connection between centromeres and ND10 proteins which can be stabilised by inhibition of proteasome-mediated proteolysis.

L3 ANSWER 30 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1998:361704 BIOSIS

DN PREV199800361704

TI Cytoplasmic forms of human T-cell leukemia virus type 1 tax induce NF-kappaB activation.
 AU Nicot, Christophe; Tie, Feng; Giam, Chou-Zen (1)
 CS (1) Dep. Microbiol. Immunol., Uniformed Services Univ. Health Sci., 4301 Jones Bridge Rd., Bethesda, MD 20814-4799 USA
 SO Journal of Virology, (Aug., 1998) Vol. 72, No. 8, pp. 6777-6784. ISSN: 0022-538X.
 DT Article
 LA English
 AB Human T-cell leukemia virus type 1 (HTLV-1) Tax targets I-kappaBalpha and I-kappaBbeta for phosphorylation, ubiquitination, and proteasome-mediated degradation, causing the nuclear translocation of NF-KB/Rel proteins and transcription induction of many cellular genes. The mechanism by which a nuclear protein such as Tax stimulates I-KB phosphorylation and degradation remains unclear. Here, we describe two cytoplasmic mutants of Tax, designated TaxDELTAN81 and TaxDELTAN109, from which the domains important for cyclic AMP response element binding factor (CREB) and serum response factor (SRF) binding and nuclear transport have been removed. These mutants were unable to trans activate from the HTLV-1 21-bp repeats or the serum response element in the c-fos promoter. In contrast, they activated NF-kappaB reporters, suggesting that activation of NF-kappaB by Tax occurs in the cytoplasm. Incorporation of the nuclear localization signal (NLS) of the simian virus 40 large T antigen into TaxDELTAN81 and TaxDELTAN109 redirected both proteins predominantly to the nucleus yet did not restore trans activation via CREB or SRF. The NLS fusion had little effect on TaxDELTAN81 but reduced NF-kappaB trans activation by TaxDELTAN109, possibly because of its proximity to the NF-kappaB-activating domain of Tax. In contrast to wild-type Tax, the cytoplasmic TaxDELTAN mutants are not cytotoxic. Stable expression of TaxDELTAN109 in HeLa cells resulted in a significant reduction in the intracellular level of I-kappaBalpha, with the constitutive presence of NF-kappaB in the nucleus and concomitant activation of the NF-kappaB enhancer. These results are suggestive of a potential application of the TaxDELTAN109-like mutants in targeting I-kappaB degradation and NF-kappaB activation. Interestingly, a Tax species with a molecular mass similar to that of TaxDELTAN109 was identified in many HTLV-1-transformed T cells, suggesting that TaxDELTAN109-like species might play a role in HTLV-1-induced leukemogenesis.

L3 ANSWER 31 OF 47 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
 AN 1998075682 EMBASE
 TI HIV-1 neutralizing antibodies in the genital and respiratory tracts of mice intranasally immunized with oligomeric gp160.
 AU VanCott T.C.; Kaminski R.W.; Mascola J.R.; Kalyanaraman V.S.; Wassef N.M.; Alving C.R.; Ulrich J.T.; Lowell G.H.; Birx D.L.
 CS Dr. T.C. VanCott, Henry M. Jackson Foundation, 13 Taft Court, Rockville, MD 20850, United States. tvancott@hiv.hjff.org
 SO Journal of Immunology, (15 Feb 1998) 160/4 (2000-2012).
 Refs: 87
 ISSN: 0022-1767 CODEN: JOIMA3
 CY United States
 DT Journal; Article
 FS 004 Microbiology
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 LA English
 SL English
 AB Because mucosal surfaces are a primary route of HIV-1 infection, we evaluated the mucosal immunogenicity of a candidate HIV-1 vaccine, oligomeric gp160 (o-gp160). In prior studies, parenteral immunization of rabbits with o-gp160 elicited broad neutralizing serum Ab responses against both T cell line-adapted HIV-1 and some primary HIV-1 isolates. In this study, nasal immunization of mice with o-gp160, formulated with liposomes containing monophosphoryl lipid A (MPL), MPL-AF,

proteosomes, emulsomes, or **proteosomes** with emulsomes elicited strong gp160-specific IgG and IgA responses in serum as well as vaginal, lung, and intestinal washes and fecal pellets. The genital, respiratory, and intestinal Abs were determined to be locally produced. No mucosal immune responses were measurable when the immunogen was given s.c. Abs from sera and from vaginal and lung washes preferentially recognized native forms of monomeric gp120, suggesting no substantial loss in protein tertiary conformation after vaccine formulation and mucosal administration. Inhibition of HIV-1(MN) infection of H9 cells was found in sera from mice immunized intranasally with o-gp160 formulated with liposomes plus MPL, **proteosomes**, and **proteosomes** plus emulsomes. Formulations of o- gp160 with MPL-AF, **proteosomes**, emulsomes, or **proteosomes** plus emulsomes elicited HIV-1(MN)-neutralizing Ab in lung wash, and formulations with **proteosomes**, emulsomes, or **proteosomes** plus emulsomes elicited HIV-1(MN)- neutralizing Ab in vaginal wash. These data demonstrate the feasibility of inducing both systemic and mucosal HIV-1-neutralizing Ab by intranasal immunization with an oligomeric gp160 protein.

L3 ANSWER 32 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1998:228643 BIOSIS

DN PREV199800228643

TI How do **viruses** evade immune response? Blocking of MHC class I molecules.

AU Wojtowicz, Radoslaw (1)

CS (1) ul. Marymoncka 99, 01-813 Warszawa Poland

SO Postepy Biologii Komorki, (1998) Vol. 25, No. 2, pp. 211-223.

ISSN: 0324-833X.

DT Article

LA Polish

SL Polish; English

AB During last few years of the studies on **viruses**, interesting results have been obtained. It appeared that some **viruses** can evade detection and elimination by host immune system in a very specific way. In this article 5 **viruses** have been presented: human cytomegalovirus, mouse cytomegalovirus, Epstein-Barr **virus**, adenovirus and herpes simplex **virus**. Each of them uses specific mechanism blocking in a different way antigen presentation on the cell surface by MHC class I molecules.

L3 ANSWER 33 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1998:32254 BIOSIS

DN PREV19980032254

TI The human papillomavirus E7 oncoprotein functionally interacts with the S4 subunit of the 26 S proteasome.

AU Berezutskaya, Ekaterena; Bagchi, Srilata (1)

CS (1) Cent. Mol. Biol. Oral Diseases, College Dentistry, Univ. Illinois at Chicago, 801 S. Paulina St., Chicago, IL 60612 USA

SO Journal of Biological Chemistry, (Nov. 28, 1997) Vol. 272, No. 48, pp. 30135-30140.

ISSN: 0021-9258.

DT Article

LA English

AB Human papillomaviruses (HPV) have been etiologically linked to human cervical cancer. More than 90% of cervical cancer tissues express two HPV-encoded oncoproteins E6 and E7. Both E6 and E7 proteins possess transformation activity, and together they cooperate to transform primary human keratinocytes, fibroblasts. and epithelial cells. The transforming activity of E7 is associated with its ability to bind the retinoblastoma tumor suppressor protein (Rb). However, the carboxyl-terminal mutants of E7 are also defective for transformation, suggesting that other cellular targets for E7 might exist. We screened a human placenta cDNA library by yeast two-hybrid assay using HPV 16 E7 as a bait and identified the

subunit 4 (S4) ATPase of the 26 S proteasome as a novel E7-binding protein. E7 binds to S4 through the carboxyl-terminal zinc binding motif, and the binding is independent of E7 sequences involved in binding to Rb. The interaction between S4 and E7 can be easily detected by in vitro protein binding assays. Moreover, we found that E7 increases the ATPase activity of S4. A recent study has shown that, in epithelial cells, E7 degrades Rb through the 26 S proteasome pathway. We hypothesize that E7 might target Rb for degradation by 26 S proteasome through its interaction with the subunit 4 of the proteasome.

L3 ANSWER 34 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:1078 BIOSIS
DN PREV199800001078
TI Inhibition of ubiquitin/proteasome-dependent protein degradation by the Gly-Ala repeat domain of the Epstein-Barr virus nuclear antigen 1.
AU Levitskaya, Jelena; Sharipo, Anatoly; Leonchiks, Ainars; Ciechanover, Aaron; Masucci, Maria G. (1)
CS (1) Microbiol. Tumor Biol. Cent., Karolinska Inst., Box 280, S-171 77 Stockholm Sweden
SO Proceedings of the National Academy of Sciences of the United States of America, (Nov. 11, 1997) Vol. 94, No. 23, pp. 12616-12621.
ISSN: 0027-8424.
DT Article
LA English
AB The Epstein-Barr virus (EBV) encoded nuclear antigen (EBNA) 1 is expressed in latently infected B lymphocytes that persist for life in healthy virus carriers and is the only viral protein regularly detected in all EBV associated malignancies. The Gly-Ala repeat domain of EBNA1 was shown to inhibit in cis the presentation of major histocompatibility complex (MHC) class I restricted cytotoxic T cell epitopes from EBNA4. It appears that the majority of antigens presented via the MHC I pathway are subject to ATP-dependent ubiquitination and degradation by the proteasome. We have investigated the influence of the repeat on this process by comparing the degradation of EBNA1, EBNA4, and Gly-Ala containing EBNA4 chimeras in a cell-free system. EBNA4 was efficiently degraded in an ATP/ubiquitin/proteasome-dependent fashion whereas EBNA1 was resistant to degradation. Processing of EBNA1 was restored by deletion of the Gly-Ala domain whereas insertion of Gly-Ala repeats of various lengths and in different positions prevented the degradation of EBNA4 without appreciable effect on ubiquitination. Inhibition was also achieved by insertion of a Pro-Ala coding sequence. The results suggest that the repeat may affect MHC I restricted responses by inhibiting antigen processing via the ubiquitin/proteasome pathway. The presence of regularly interspersed Ala residues appears to be important for the effect.

L3 ANSWER 35 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:157606 BIOSIS
DN PREV199799456809
TI Misfolded major histocompatibility complex class I heavy chains are translocated into the cytoplasm and degraded by the proteasome.
AU Hughes, Eric A.; Hammond, Craig; Cresswell, Peter (1)
CS (1) Section Immunobiol., Howard Hughes Med. Inst., Yale Univ. Sch. Med., 310 Cedar St., New Haven, CT 06510 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 5, pp. 1896-1901.
ISSN: 0027-8424.
DT Article
LA English
AB N-acetyl-L-leucyl-L-leucyl-L-norleucinal (LLnL), which reversibly inhibits the proteasome in addition to other proteases, and a more specific irreversible inhibitor of the proteasome, lactacystin, were found to cause the accumulation of major histocompatibility complex (MHC) class I heavy

chains in the cytosol of the beta-2-microglobulin-deficient cell line Daudi and the TAP-deficient cell line .174. These cell lines, which are severely impaired in their ability to fold MHC class I heavy chain, showed an accumulation of soluble class I heavy chains at different rates over a period of hours in the presence of LLnL. The accumulation of soluble class I heavy chains in the presence of either LLnL or lactacystin was easily revealed in Daudi and .174 but almost undetectable in a Daudi transfectant expressing beta-2-microglobulin and in 45.1, the wild-type parent of .174. The soluble class I heavy chain was also found to be devoid of its N-linked glycan and to be located in the cytosol. When the gene for ICP47, a herpes simplex virus protein that blocks the translocation of peptides into the endoplasmic reticulum, was transfected into 45.1, a similar accumulation of soluble MHC class I heavy chain was detectable. These data suggest that in cells where the MHC class I molecule is unable to assemble properly, the misfolded heavy chain is removed from the endoplasmic reticulum to the cytosol, deglycosylated, and degraded by the proteasome.

L3 ANSWER 36 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE
7

AN 1997:320833 BIOSIS

DN PREV199799611321

TI The ER-luminal domain of the HCMV glycoprotein US6 inhibits peptide translocation by TAP.

AU Ahn, Kwangseog; Gruhler, Albrecht; Galocha, Begona; Jones, Thomas R.; Wiertz, Emmanuel J. H. J.; Ploegh, Hidde L.; Peterson, P. A.; Yang, Young (1); Fruh, Klaus (1)

CS (1) R.W. Johnson Pharm. Res. Inst., 3535 General Atomics Court, Suite 100, San Diego, CA 92121 USA

SO Immunity, (1997) Vol. 6, No. 5, pp. 613-621.

ISSN: 1074-7613.

DT Article

LA English

AB Human cytomegalovirus (HCMV) inhibits MHC class I antigen presentation by a sequential multistep process involving a family of unique short (US) region-encoded glycoproteins. US3 retains class I molecules, whereas US2 and US11 mediate the cytosolic degradation of heavy chains by the **proteasomes**. In US6-transfected cells, however, intracellular transport of class I molecules is impaired because of defective peptide translocation by transporters associated with antigen processing (TAP). Peptide transport is restored in HCMV mutants lacking US6. In contrast to the cytosolic herpes simplex virus protein ICP47, US6 interacts with TAP inside the endoplasmic reticulum lumen, as shown by US6 derivatives lacking the transmembrane and cytoplasmic domains and by the observation that US6 does not prevent peptides from binding to TAP. Thus, HCMV targets TAP for immuneescape by a molecular mechanism different from that of herpes simplex virus.

L3 ANSWER 37 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1997:118996 BIOSIS

DN PREV199799425499

TI The hepatitis B virus X protein: The quest for a role in viral replication and pathogenesis.

AU Seeger, Christoph

CS Inst. Cancer Res., Fox Chase Cancer Cent., Philadelphia, PA USA

SO Hepatology, (1997) Vol. 25, No. 2, pp. 496-498.

ISSN: 0270-9139.

DT Article

LA English

AB Although the biological importance of hepatitis B virus X protein (HBX) in the life cycle of hepatitis B virus has been well established, the cellular and molecular basis of its function remains largely undefined. Despite the association of multiple activities with HBX, none of them appear to provide a unifying hypothesis regarding the

true biological function of HBX. Identification and characterization of cellular targets of HBX remain an essential goal in the elucidation of the molecular mechanisms of HBX. Using the *Saccharomyces cerevisiae* two-hybrid system, we have identified and characterized a novel subunit of the proteasome complex (XAPC7) that interacts specifically with HBX. We also showed that HBX binds specifically to XAPC7 in vitro. Mutagenesis studies have defined the domains of interaction to be critical for the function of HBX. Furthermore, overexpression of XAPC7 appeared to activate transcription by itself and antisense expression of XAPC7 was able to block transactivation by HBX. Therefore, the proteasome complex is possibly a functional target of HBX in cells.

L3 ANSWER 38 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE
8
AN 1997:107153 BIOSIS
DN PREV199799406356
TI **Proteosomes**, emulsomes, and cholera toxin B improve nasal immunogenicity of human immunodeficiency virus gp160 in mice: Induction of serum, intestinal, vaginal, and lung IgA and IgG.
AU Lowell, George H.; Kaminski, Robert W.; Vancott, Thomas C.; Slike, Bonnie; Kersey, Kathryn; Zawoznik, Eduardo; Loomis-Price, Lawrence; Smith, Gale; Redfield, Robert R.; Amselem, Shimon; Birx, Deborah L.
CS Intellivax Inc. 6303 Western Run Dr., Baltimore, MD 21215 USA
SO Journal of Infectious Diseases, (1997) Vol. 175, No. 2, pp. 292-301.
ISSN: 0022-1899.

DT Article

LA English

AB Intranasal immunization of mice with human immunodeficiency virus (HIV) rgp160 complexed to **proteosomes** improved anti-gp160 serum IgA and IgG titers, increased the number of gp160 peptides recognized, and stimulated anti-gp160 intestinal IgA compared with immunization with uncomplexed rgp160 in saline. These enhanced responses were especially evident when either a bioadhesive nanoemulsion (emulsomes) or cholera toxin B subunit (CTB) was added to the **proteosome**-rgp160 vaccine. Furthermore, anti-gp160 IgG and IgA in vaginal secretions and fecal extracts were induced after intranasal immunization with **proteosome**-rgp160 delivered either in saline or with emulsomes. Formulation of uncomplexed rgp160 with emulsomes or CTB also enhanced serum and selected mucosal IgA responses. Induction of serum, vaginal, bronchial, intestinal, and fecal IgA and IgG by intranasal **proteosome**-rgp160 vaccines delivered in saline or with emulsomes or CTB is encouraging for mucosal vaccine development to help control the spread of HIV transmission and AIDS.

L3 ANSWER 39 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:353958 BIOSIS
DN PREV199799660361
TI Computer simulations to identify in polyproteins of FMDV OK1 and A12 strains putative nonapeptides with amino acid motifs for binding to BoLA class I A11 and A20 haplotype molecules.
AU Becker, Yechiel
CS Dep. Mol. Virol., Inst. Microbiol., Fac. Med., Hebrew Univ. Jerusalem, Jerusalem Israel
SO Virus Genes, (1997) Vol. 14, No. 2, pp. 123-129.
ISSN: 0920-8569.

DT Article

LA English

AB The computer program "Findpatterns" was used to search FMDV- (OK1 and A12 strains) coded structural and nonstructural proteins for the availability of putative proteasome-generated nonapeptides with motifs reported for BoLA class I A11 and A20 haplotypes. These BoLA class I A11 and A20 nonapeptide motifs are identical to motifs of nonapeptides that interact with the peptide binding grooves of HLA class I B35 and B27 haplotypes, respectively. The computer findpattern program was used to analyze the

FMDV-coded polyproteins for proteolytically cleavable nonapeptides with motifs for binding to the peptide binding grooves of BoLA class I A11 or 20 haplotypes. The computer simulations revealed that FMDV-infected cells (keratinocytes and antigen presenting cells, e.g., dendritic Langerhans cells in bovines) may be able to present viral nonapeptides to CD8+ cytolytic T cells (CTLs) in a BoLA-restricted manner. The role of the cellular arm of the immune response in the protection of bovines against FMDV is not known. Thus, the present computer analysis may encourage further experiments to develop a new generation of FMDV nonapeptide vaccines to stimulate the anti-FMDV cytolytic T cell response in bovine so this would complement the humoral immune response achieved by immunization with the inactivated virus vaccine.

- L3 ANSWER 40 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1997:21568 BIOSIS
 DN PREV199799320771
 TI Sec61-mediated transfer of a membrane protein from the endoplasmic reticulum to the proteasome for destruction.
 AU Wiertz, Emmanuel J. H. J.; Tortorella, Domenico; Bogyo, Matthew; Yu, Joyce; Mothes, Walther; Jones, Thomas R.; Rapoport, Tom A.; Ploegh, Hidde L. (1)
 CS (1) Cent. Cancer Res., Dep. Biol., Massachusetts Inst. Technol., Cambridge, MA 02139 USA
 SO Nature (London), (1996) Vol. 384, No. 6608, pp. 432-438.
 ISSN: 0028-0836.
 DT Article
 LA English
 AB The human cytomegalovirus genome encodes proteins that trigger destruction of newly synthesized major histocompatibility complex (MHC) class I molecules. The human cytomegalovirus gene US2 specifies a product capable of dislocating MHC class I molecules from the endoplasmic reticulum to the cytosol and delivering them to the proteasome. This process involves the Sec61 complex, in what appears to be a reversal of the reaction by which it translocates nascent chains into the endoplasmic reticulum.
- L3 ANSWER 41 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE
 9
 AN 1996:26493 BIOSIS
 DN PREV199698598628
 TI Intranasal immunization of mice against influenza with synthetic peptides anchored to **proteosomes**.
 AU Levi, Raphael; Aboud-Pirak, Esther; Leclerc, Claud; Lowell, George H.; Arnon, Ruth (1)
 CS (1) Dep. Chem. Immunol., Weizmann Inst. Sci., Rehovot 76100 Israel
 SO Vaccine, (1995) Vol. 13, No. 14, pp. 1353-1359.
 ISSN: 0264-410X.
 DT Article
 LA English
 AB Synthetic vaccines that are based on peptides representing immunogenic epitopes require a carrier molecule as well as an adjuvant in order to be effective. The choice of carriers or adjuvants approved for use in humans is very limited, and a considerable effort is devoted to develop new and efficient delivery systems. One of these vehicles utilizes preparations of outer membranes of meningococci, that form hydrophobic interactions, denoted **proteosomes**. Immunogenic proteins and peptides can be anchored to these **proteosomes** vesicles, which may serve as both carrier and adjuvant functions. In the present study we examined the ability of **proteosomes** to present epitopes of influenza, to elicit specific anti-influenza responses and to protect mice against viral challenge after intranasal immunization. Three influenza peptides were used-one corresponding to amino acid residues 91-108 of the haemagglutinin surface glycoprotein of H3 subtype, which comprises a B-cell epitope, and two from the internal nucleoprotein-a T-helper cell (Th) epitope (residues 55-69) and a cytotoxic T-lymphocyte (CTL) epitope (147-158). Mice were

immunized intranasally (i.n.) with preparations containing each of the above epitopes, or various combinations thereof. The results obtained with this system demonstrate that influenza epitopes represented by synthetic peptides anchored to a **proteosome** carrier elicit both humoral and cellular specific immune responses, that can lead to partial protection of the mice from viral challenge. The importance of immunizing with vaccines containing both B- and T-cell peptide epitopes was emphasized by the demonstration that such vaccines elicited longer lasting immunity and led to more effective protection against influenza viral challenge.

L3 ANSWER 42 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1995:190216 BIOSIS
 DN PREV199598204516
 TI Mucosal immunogenicity and efficacy of **proteosome** and PA adjuvants for HIV, influenza, shigella and staph. enterotoxin B (SEB) vaccines.
 AU Lowell, G. (1); Kaminski, R. (1); Colleton, C. (1); Orr, N.; Mallett, C. (1); Levi, R.; Aboud-Pirak, E.; Estep, J.; Pitt, L.; Loomis, L. (1); Kersey, K. (1); Vancott, T. (1); Baker, W. (1); Frost, D. (1); Hunt, R.; Hatch, J.; Dean, S. (1); Amselem, S.; Smith, G.; Cohen, D.; Arnon, R.; Redfield, R. (1); Bix, D. (1); Hale, T. (1); Baze, W. (1)
 CS (1) Walter Reed Army Inst. Res., Washington, DC USA
 SO Journal of Cellular Biochemistry Supplement, (1995) Vol. 0, No. 19A, pp. 259.
 Meeting Info.: Keystone Symposium on Mucosal Immunity: New Strategies for Protection Against Viral and Bacterial Pathogens Keystone, Colorado, USA January 16-23, 1995
 ISSN: 0733-1959.
 DT Conference
 LA English

L3 ANSWER 43 OF 47 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
 AN 96065442 EMBASE
 DN 1996065442
 TI HIV peptide and protein antibody responses elicited by immunization with rgp160 formulated with **proteosomes**, alum, and/or submicron emulsions.
 AU Kaminski R.W.; Loomis L.; Levi M.; Amselem S.; Kersey K.; VanCott T.; Yogev A.; Friedman D.; Smith G.; Wahren B.; Redfield R.; Bix D.; Lowell G.H.
 CS Intellivax Inc, 6303 Western Run Dr, Baltimore, MD 21215, United States
 SO Vaccine Research, (1995) 4/4 (189-206).
 ISSN: 1056-7909 CODEN: VAREES
 CY United States
 DT Journal; Article
 FS 004 Microbiology
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 LA English
 SL English
 AB The parenteral immunogenicity in mice and rabbits of HIV recombinant protein rgp160 prior to and following noncovalent complexing to meningococcal outer membrane protein **proteosomes** was examined. **Proteosome**-complexed and free rgp160 were administered in saline, with alum and/or intrinsic or extrinsic formulations of a submicron emulsion (SME) adjuvant. **Proteosome**-rgp160 vaccines administered in saline, with alum or in an intrinsic SME formulation, increased the intensity and quantity of peptide specific immune responses in mice and rabbits compared to uncomplexed rgp160 given either in saline or adsorbed to alum. Immunizing rabbits with intrinsically formulated SME vaccines containing either rgp160 or **proteosome**-rgp160 increased serum antiprotein ELISA antibody levels and broadened the number of peptides recognized. These data show that both quantitative and qualitative

improvement of peptide and/or protein antibody responses can be achieved by altering the formulation of rgp160 to include alternative vaccine delivery and adjuvant preparations such as **proteosomes** and an intrinsic SME. These results are encouraging for the development of new formulations of subunit vaccines to enhance or alter humoral responses to peptide epitopes of large recombinant proteins and may be applicable to an improved new generation envelope vaccine for HIV therapy or prevention.

- L3 ANSWER 44 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1995:149099 BIOSIS
 DN PREV199598163399
 TI Nasal immunization with HIV gp160 formulated with **proteosomes**, emulsomes and/or cholera toxin B subunit: Induction of anti-gp160 serum IgA and IgG and intestinal, vaginal and lung IgA.
 AU Lowell, G. H. (1); Kaminski, R.; Kersey, K.; Vancott, T. (1); Loomis, L.; Smith, G.; Redfield, R. (1); Freidman, D.; Amselem, S.; Bix, D. (1)
 CS (1) Walter Reed Army Inst. Res., Washington, DC USA
 SO AMERICAN SOCIETY FOR MICROBIOLOGY.. (1995) pp. 81. Human retroviruses and related infections.
 Publisher: American Society for Microbiology (ASM) Books Division, 1325 Massachusetts Ave. NW, Washington, DC 20005-4171, USA.
 Meeting Info.: 2nd National Conference Washington, D.C., USA January 29-February 2, 1995
 ISBN: 1-55581-097-7.
 DT Conference
 LA English
- L3 ANSWER 45 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1994:330941 BIOSIS
 DN PREV199497343941
 TI Parenteral or intranasal immunization with HIV gp160 formulated with **proteosomes** and/or PA adjuvants enhances epitope-specific IgG or IgA.
 AU Kaminski, R. (1); Amselem, S.; Levi, M.; Loomis, L.; Kersey, K.; Vancott, T.; Friedman, D.; Smith, G.; Wahren, B.; Redfield, R.; Bix, D.; Lowell, G.
 CS (1) Walter Reed Army Inst. Res., Washington, DC USA
 SO Abstracts of the General Meeting of the American Society for Microbiology, (1994) Vol. 94, No. 0, pp. 155.
 Meeting Info.: 94th General Meeting of the American Society for Microbiology Las Vegas, Nevada, USA May 23-27, 1994
 ISSN: 1060-2011.
 DT Conference
 LA English
- L3 ANSWER 46 OF 47 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 10
 AN 92322516 EMBASE
 DN 1992322516
 TI Immunopotentiating reconstituted influenza virosomes (IRIVs) and other adjuvants for improved presentation of small antigens.
 AU Gluck R.
 CS Department of Virology, Swiss Serum and Vaccine Institute, PO Box 2707, CH-3001 Berne, Switzerland
 SO Vaccine, (1992) 10/13 (915-919).
 ISSN: 0264-410X CODEN: VACCDE
 CY United Kingdom
 DT Journal; Conference Article
 FS 004 Microbiology
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 LA English
 SL English
 AB Synthetic peptides, purified subunits or inactivated small **virus** particles require immunopotentialiation if they are to be effective vaccines.

A large range of procedures to enhance immunogenicity has evolved over the last decades: aluminium salts, **proteosomes**, immunostimulating complexes (ISCOMs), liposomes, conjugation with bacterial products or derivatives, combination with surface-active agents or application of cytokines have been the most described classes of adjuvants. We describe here the design of an inactivated hepatitis A vaccine adjuvanted with immunopotentiating reconstituted influenza virosomes (IRIVs). The formalin-inactivated hepatitis A particles are attached to reconstituted protein-lipid complexes consisting of a mixture of phospholipids and influenza **virus** glycoproteins. With this new vaccine design we combined different immunostimulating effects: immunopotentiality by phospholipid vesicles, recognition of the haemagglutinin (HA) epitopes by the immune system, binding capacity of HA to sialic acid-containing receptors of macrophages and immunocompetent cells and mediation of entry into the cytoplasm of macrophages by a membrane-fusion event triggered by HA. Hepatitis A seronegative human volunteers received one intramuscular injection with this new vaccine. There were only few mild local reactions and 14 days after vaccination 100% of the subjects were seropositive. Among the individuals (control group) who received an alum-adsorbed vaccine, 88% developed local reactions. The seroconversion rate was 44%. We conclude from these results that the IRIVs provide a new approach to the future design of adjuvanted vaccines.

L3 ANSWER 47 OF 47 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE
11
AN 1992:28040 BIOSIS
DN BA93:17315
TI THE COMPLEX OF FLAVIVIRUS ENVELOPE POLYPEPTIDE WITH MENINGOCOCCAL
PROTEOSOMES ELICITS FORMATION OF **VIRUS-NEUTRALIZING**
ANTIBODIES.
AU SLAVIK I; KUZEMENSKA P; KOZUCH O; MATOSKA J; POKORNY J; SEKEYOVA M
CS INST. VIROL., SLOVAK ACAD. SCI., 842 46 BRATISLAVA, CZECH.
SO ACTA VIROL (PRAGUE) (ENGL ED), (1991) 35 (4), 313-321.
CODEN: AVIRA2. ISSN: 0001-723X.
FS BA; OLD
LA English
AB Polypeptide E of tick-borne encephalitis **virus** was isolated in
sucrose density gradient and mixed with equal weight portion of
meningococcal **proteosomes** in the presence of
N-dodecyl-N,N-dimethylglycine. Mutual complexing of viral and bacterial
molecules occurred after removal of detergent by dialysis. Complexed
particles appeared in the electron microscope as 40-50 .mu.m thick
short-rod structures covered on their surface with both, delicate
poppy-like grains, or envelope subunit-like clustered molecules. Even when
applied without adjuvant, the complex of tick-borne encephalitis
virus polypeptide E with meningococcal **proteosomes**
elicited in mice a marked antiviral as well as antibacterial humoral
response.